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pathway of *S. fradiae* (S49054) (SEQ ID NO:116). Given in parentheses are protein accession numbers. The $\alpha\beta\alpha$ fold with the NAD^+ -binding motif of GxGxxG is boxed.--

In accordance with 37 CFR §1.121 a marked up version of the above-amended paragraph(s) illustrating the changes introduced by the forgoing amendment(s) are provided in Appendix C.

REMARKS

This amendment is provided in Response to the Notice to Comply With Requirements for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant(s) request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing the sequences (SEQ ID NOs:1-118) in computer readable form, and a paper copy of the sequence information that has been printed from the floppy disk.

The information contained in the computer readable form (floppy disk) was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy.

This amendment contains no new matter. The amendments to the specification and/or claims are to provide a formal sequence listing and/or to provide appropriate cross-references to SEQ ID Numbers in accordance with 37 C.F.R. §§1.821 to 1.825. The sequence information provided herein finds support in the specification as filed.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 337-7871.

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Respectfully submitted,



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APPENDIX A
VERSION WITH MARKINGS TO SHOW CHANGES MADE IN 09/478,188 WITH ENTRY
OF THIS AMENDMENT

In the specification:

Table II at page 18:

Table II. C-1027 gene cluster open reading frames (27 to 42), primers for ORF amplification, and proposed functions

ORF	Relative Position	Primers	Function	SEQ ID NO.
orf-27	43945-46023	Fwd: GTG TGC CCG GTG ACA GAC	Antibiotic	71
		Rev: TCA GCC CAC GGG CTG GGA	Transporter	72
orf-28	46167-47171	Fwd: GTG TTG GGC GAT GAG GAC	O-	73
		Rev: TCA GAC CGC GGA CAT CTG	methyltransferase	74
orf--29	47227-48485	Fwd: ATG GCC GGC CTG GTC ATG	p450	75
		Rev: TCA GGA CCC GAG GGT CAC	hydroxylase	76
orf-30	48610-49714	Fwd: GTG GAC CAG ACG TCT ACG	Oxidoreductase	77
		Rev: TCA TGC AGG TGC AGC GTG		78
orf-31	50350-51390	Fwd: ATG AGG CCG CTC GTT CGG	Unknown	79
		Rev: TCA TCC CGG CCC GGC GGC	Protein	80
orf-32	51420-52341	Fwd: ATG AGA ACG CGG CGA CGC	Oxidoreductase	81
		Rev: TCA CGG CCG GAG GCG TAC		82
orf-33	53241-54074	Fwd: GTG TAT CAG CCG GAC TGT	Unknown	83
		Rev: CTA CTC ATT CCA GTT GTG	Protein	84
orf-34	54230-55379	Fwd: ATG TCT ACG GGC TAT CTC	Unknown	85
		Rev: TCA GCC GCC GGT GGC GCC	Protein	86
orf-35	56027-56881	Fwd: ATG TTC TCC CCC GCC GCC	Oxidase/	87
		Rev: TCA GTA CGC CTG GTG GGC	Dehydrogenase	88
orf-36	56928-57730	Fwd: ATG AAT TCG CTC GAC GAC	Unknown	89
		Rev: TCA GCT CCC GGT CGC CGC	Protein	90
orf-37	57834-58304	Fwd: ATG ACC GCG ACG AAT CCT	Regulatory	91
		Rev: CTA GGC GGC GCG TCC CGC		92
orf-38	58440-60091	Fwd: ATG AGC ACC ACG GCC GAG	Oxidoreductase	93
		Rev: TCA GCC GCG CGC CGA CGG		94
orf-39	60092-60622	Fwd: ATG ACC CTG GAG GCC TAC	Regulatory	95
		Rev: TCA TGC GGG GCT CCC GGT		96
orf-40	60940-62020	Fwd: GTG AAA AGT GAC TCT GCC	Regulatory	97
		Rev: TCA ACG GCG AGT TGG CTG		98
orf-41	62045-62899	Fwd: GTG ACC ACG AAC ACC ATC	Regulatory	99
		Rev: TCA CCC GCG ATC TCG ATC		100
orf-42	62788-63164	Fwd: (partial ORF)	p450	101
		Rev: TCA CCT CGC CGT ACT CAC	hydroxylase	[102]

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Page 41, lines 3-25:

For type II PKS, the following two pairs of degenerate primers were used—5'-AGC TCC ATC AAG TCS ATG RTC GG-3' (forward, SEQ ID NO:102[103]) / 5'-CC GGT GTT SAC SGC GTA GAA CCA GGC G-3' (reverse, SEQ ID NO:103[104]) and 5'-GAC ACV GCN TGY TCB TCV-3' (forward, SEQ ID NO:104[105]) / 5'-RTG SGC RTT VGT NCC RCT-3' (SEQ ID NO:105[106]) (B, C+G+T; N, A+C+G+T; R, A+G; S, C+G; V, A+C+G; Y, C+T) (reverse) (Seow *et al.* (1997) *J. Bacteriol.*, 179: 7360-7368). No product was amplified under all conditions tested. For type I PKS, the following pair of degenerate primers were used—5'-GCS TCC CGS GAC CTG GGC TTC GAC TC-3' (forward, SEQ ID NO:106[107]) / 5'-AG SGA SGA SGA GCA GGC GGT STC SAC-3' (S, G+C) (reverse, SEQ ID NO:107[108]) (Kakavas *et al.* (1997) *J. Bacteriol.*, 179: 7515-7522). A distinctive product with the predicted size of 0.75 kb was amplified in the presence of 20% glycerol and cloned into pGEM-T according to the protocol provided by the manufacturer (Promega) to yield pBS1001.

For NGDH, the following pair of degenerate primers were used—5'-CS GGS GSS GCS GGS TTC ATC GG-3' (forward, SEQ ID NO:108[109]) / 5'-GG GWR CTG GYR SGG SCC GTA GTT G-3' (R, A+G; S, C+G; W, A+T; Y, C+T) (reverse, SEQ ID NO:109[110]) (Decker, *et al.* (1996) *FEMS Lett.*, 141: 195-201). A distinctive product with the predicted size of 0.55 kb was amplified and cloned into pGEM-T to yield pBS1002.

For *cagA*, the following pair of primers, flanking its coding region, were used—5'-AG GTG GAG GCG CTC ACC GAG-3' (forward, SEQ ID NO:110[111]) / 5'-G GGC GTC AGG CCG TAA GAA G-3' (reverse, SEQ ID NO:111[112]) (Sakata *et al.* (1992) *Biosci. Biotechnol. Biochem.*, 56: 159201595). A distinctive product with the predicted size of 0.73 kb was amplified from pBS1005 and cloned into pGEM-T to yield pBS1003.

Page 14, lines 11-22:

--Figure 6 shows the DNA (SEQ ID NO:112) and deduced amino acid sequences of the 3.0-kb *Bam*HI fragment from pBS1007, showing the *sgcA* (SEQ ID NO:113) and *sgcB* genes (SEQ ID NO:114). Possible RBSs are boxed. The presumed translational start and stop sites are in boldface. Restriction enzyme sites of interest are underlined. The amino acids, according to which the degenerated PCR primer were designed for amplifying the dNDP-glucose 4,6-dehydratase gene from *S. globisporus*, are underlined.

Figure 7 shows the amino acid sequence alignment of SgcA (**SEQ ID NO:113**) with three other dNDP-glucose 4,6-dehydratases. Gdh, TDP-glucose 4,6-dehydratase of *S. erythraea* (AAA68211) (**SEQ ID NO:115**); MtmE, TDP-glucose 4,6-dehydratase in the mithramycin pathway of *S. argillaceus* (CAA71847) (**SEQ ID NO:117**); TylA2, TDP-glucose 4,6-dehydratase in the tylosin pathway of *S. fradiae* (S49054) (**SEQ ID NO:116**). Given in parentheses are protein accession numbers. The $\alpha\beta\alpha$ fold with the NAD⁺-binding motif of GxGxxG is boxed.--

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